IRB Study #: 04-1677 (CTRC#2067)

Study Title: Physiological Changes in Adults with Metabolic Syndrome Exposed to Concentrated Ultrafine Chapel Hill Air Particles

PI: Robert Devlin, PhD

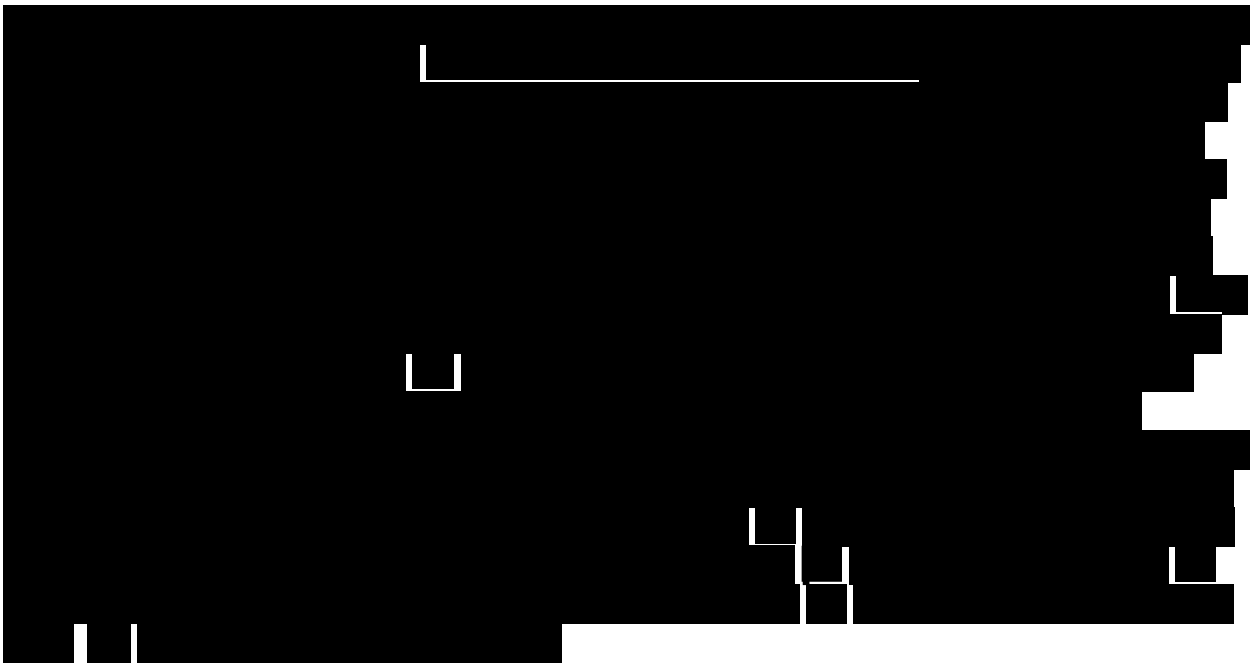
Sponsor: EPA

The Adverse event took place 10-7-2010 at the EPA Human Studies Facility on the UNC-CH campus

The volunteer (subject XCE-227) reported to EPA facility on [redacted] to participate in the first of two exposure sessions for IRB#04-1677. The volunteer had previously undergone the same exposures for this protocol two years ago. The study progressed as expected and the volunteer entered the exposure chamber at 11:21am. All vitals were being monitored during the chamber exposure and were normal and consistent. The subject was reading and operating a remote control while in the chamber, which was contributing to several alarms being set off by the ECG for noise and the pulse oximeter for loss of tracing, this was noted by the investigator at the chamber, [redacted], to be occurring due to physical movement of the subject's arms and fingers. At 11:44 automatic alarms sounded at the chamber consol and the medical station and an automatic ECG printout of an event was printed in the medical station. The subject's ECG reading indicated a 22 beat supraventricular tachycardia (SVT) lasting 10.5 seconds with 124bpm. After 10 seconds the subject's heart rate and rhythm were normal and all other vitals remained normal, the subject reported [redacted] was feeling fine. The study nurse, Maryann Bassett, consulted with the on-duty doctor, [redacted] (UNC) and an EPA doctor, Dr. Andy Ghio and the decision was made to remove the subject from the chamber. Nurse Bassett proceeded to the exposure chamber to observe the subject and inform the investigator at the chamber, [redacted] that a decision was made to terminate the exposure as a precautionary measure. The subject was calmly informed the exposure would be ending. The exposure was stopped at 12:08 and the subject exited the chamber at 12:10pm and returned to the medical station to rest and be consulted with Nurse Bassett and Dr.Ghio.

Nurse Bassett removed the subject's ambulatory ECG (holter) monitor to review [redacted] heart rhythm prior to and during the exposure (meanwhile the subject's vitals were being monitored by telemetry), this holter monitor normally records for 24hrs. It was found that the subject had two arrhythmia events prior to entering the chamber, while in transit and not being monitored by the medical station's real-time telemetry. The first event occurred at 10:30am 3 beat SVT 133bpm, which occurred while the subject was walking and returning from the BAU at the CTRC. Another event was noted at 11:11am, 9 beat SVT for 3.68 sec 135bpm, while the subject was putting on the facemask and waiting to enter the

exposure chamber. It was also noted that the subject had a high number of premature atrial contractions (PACs) throughout [redacted] visit.



Nurse Bassett spoke with the subject the following day, [redacted] and [redacted] said [redacted] had been admitted and observed overnight and the cardiologist said everything looked relatively normal. [redacted] was to undergo an echocardiogram (and possibly a stress test) later that day and would then let the doctor determine if [redacted] should go for the cardiologist appointment that had been made (by Dr.Ghio at the EPA) for that afternoon. The results from the echocardiogram showed no major cardiovascular issues. The subject was very thankful for the safety measures that were taken at the EPA.

It is our summation that this subject had an underlying arrhythmia, atrial irritability or other pathology that was not observed during [redacted] recent physical (date) (with ___ min of ECG readings), and [redacted] should have been excluded from participating in the study. Additionally of note, in [redacted] previous XCON exposures 2 years ago (with 24hrs of ECG monitoring) these arrhythmia arrhythmias were not present. Arrhythmias during PM exposures are not an Unanticipated Problem, however the length or severity in this cases classifies as an Adverse Event, since it was an "unfavorable medical occurrence" and is being filed with the UNC IRB. We can only conclude that the atrial fibrillation and atrial flutter were possibly related to the research , however they could also be related to the presence an underlying arrhythmias. There were no deviations from the IRB protocol and all safety measures were taken and in place. An Adverse Event report is being filed with the UNC IRB at this time.

There is always room for improvement, and the following recommendations for improvement and safety:

-To further evaluate any possible arrhythmias or underlying heart conditions of enrolled XCON subjects, they will be evaluated after 24hr holter monitoring before their exposure date.

-Automatic ECG printouts at the exposure chamber, if the heart rate is over 120bpm or other arrhythmias are detected

-CPR training for individuals sitting at the chamber consol

-Basic training for ECG and heart rhythm monitoring for individuals sitting at the chamber consol